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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/598,965

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Jean Garipey

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EXAMINER

STEELE, AMBER D

ART UNIT

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1639

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/598,965	<b>Applicant(s)</b> GARIEPY ET AL.	
	<b>Examiner</b> AMBER D. STEELE	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-35 is/are pending in the application.
- 4a) Of the above claim(s) 8-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 September 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1-23 were filed on September 15, 2006.

The preliminary amendment filed on September 15, 2006 amended claims 3, 7, 16-18, and 23.

The amendment to the claims received on April 24, 2009 amended claims 1, 2, 4-6, 8, 9, and 11-18 and added new claims 24-35.

The amendment to the claims received on November 24, 2009 amended claims 1, 4, 5, 8, 9, 11, 12, 30, and 31 and canceled claim 6.

Claims 1-5 and 7-35 are currently pending.

Claims 1-5 and 7 are currently under consideration.

### ***Election/Restrictions***

2. Applicants elected, with traverse, Group I (claims 1-7) in the reply filed on April 24, 2009. Claims 8-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

### ***Potential Rejoinder***

3. Applicants elected claims directed to the product. If the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are

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governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all the criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See “Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b),” 1184 O.G. 86 (March 26, 1996). **Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to a rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

#### ***Priority***

4. The present application claims status as a 371 (National Stage) of PCT/CA04/00443.

#### ***Sequence Compliance***

5. The application is currently in compliance with the sequence rules.

***Invention as Claimed***

6. A combinatorial protein library comprising a plurality of protein species, each protein species comprising an A chain of an ABx toxic protein into which an insert has been introduced, wherein the A chain of the ABx toxic protein comprises a protease-sensitive loop or region into which the insert has been introduced, and wherein the insert is a polypeptide of varying amino acid sequence having a length of at least 2 amino acid residues and variations thereof.

**Withdrawn Objections**

7. The objection to the drawings regarding sequences without proper SEQ ID NOs: is withdrawn in view of the amendments received on November 24, 2009.

8. The objection to the disclosure regarding sequences without proper SEQ ID NOs: is withdrawn in view of the amendments received on November 24, 2009.

9. The objection to the disclosure regarding SEQ ID NO: 1 is withdrawn in view of the amendments received on November 24, 2009.

**Maintained Objections**

***Specification***

10. The abstract of the disclosure is objected to because figures or drawings should not be duplicated in the specification (i.e. including the abstract). Figure 1 is duplicated in the abstract. Correction is required. See MPEP § 608.01(b).

***Arguments and Response***

11. Applicants contend that the abstract was amended. However, an amendment to the abstract was not found in the reply received on November 24, 2009.

**Withdrawn Rejections**

12. The rejections of claim 6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of the claim in the amendment received on November 24, 2009.

13. The rejection of claims 1-3 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Williams et al. U.S. Patent 6,080,400 issued June 27, 2000 is withdrawn in view of the claim amendments received on November 24, 2009.

14. The rejection of claims 1-3 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Gariepy et al. WO 99/40185 published August 12, 1999 (provided by applicants in the IDS) is withdrawn in view of the claim amendments received on November 24, 2009.

**Maintained Rejections**

***Claim Rejections - 35 USC § 112***

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

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regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, do the claims require the full-length sequence of SEQ ID NO: 1 with an insert at the designated positions or if only a portion of SEQ ID NO: 1 is required by the claims? Furthermore, it is not clear from the claim how much of the structure of SEQ ID NO: 1 is required to “retain catalytic activity” of the A1 domain and how much of the A2 domain is required to introduce the insert between amino acids 248 and 267 or between amino acids 251 and 252. Therefore, the scope of the presently claimed invention is not clear.

### ***Arguments and Response***

17. Applicants’ arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claims 4 and 5 were considered but are not persuasive for the following reasons.

Applicants contend that it is clear from the claims that the full-length sequence of SEQ ID NO: 1 is not required.

Applicants’ arguments are not convincing since the claim language is not clear. The claim language should be amended to clarify the scope of the present claim (e.g. how much of SEQ ID NO: 1 is necessary to “retain catalytic activity” and allow for the insert, etc.).

### ***Double Patenting***

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

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*Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-5 and 7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 129-145 of copending Application No. 12/088,206. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 12/088,206 are drawn to combinatorial protein libraries comprising an A chain of a toxic proteins and an insert of at least 2 amino acid residues wherein the A chain is from Shiga-like toxin and the insert is between residues 242 and 261 of Shiga-like toxin A chain. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Arguments and Response***

20. Applicants' arguments directed to the provisional rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 12/088,206 for claims 1-5 and 7 were considered but are not persuasive for the following reasons.

Applicants request that the provisional rejection be held in abeyance.

Applicants' arguments are not convincing since the claimed invention of 12/088,206 renders obvious the product of the instant claims. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held



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in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

**New Rejections Necessitated by Amendment**

***Claim Rejections - 35 USC § 102***

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

22. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Keener et al. U.S. Patent Application Publication 2002/0094334.

For present claims 1, 3, and 7, Keener et al. teach variants of AB toxins wherein an insert is present in the protease-sensitive loop, the insert is any length including 12 amino acids long, and the AB toxin can be Shiga-like toxin (please refer to the entire specification particularly the abstract; paragraphs 6, 14, 17, 30, 31, 40, 44, 50, and 53; Examples).

Therefore, the presently claimed product is anticipated by the teachings of Keener et al.

23. Claims 1-2 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Borgford U.S. Patent 7,375,186 filed March 24, 2003 (effective filing date of April 30, 1997).

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For present claims 1-2 and 7, Borgford teaches libraries of AB toxins wherein an insert is introduced into the protease-sensitive region (please refer to the entire specification particularly the abstract; columns 6-8, 17, 22, 23, 25, 26).

Therefore, the teachings of Borgford anticipate the presently claimed invention.

***Claim Rejections - 35 USC § 103***

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keener et al. U.S. Patent Application Publication 2002/0094334 and et al. WO 99/40185 published August 12, 1999 (provided by applicants in the IDS).

For present claims 1, 3-5, and 7, Keener et al. teach variants of AB toxins wherein an insert is present in the protease-sensitive loop (insert amino acids into natural, exposed loops of A chain, see paragraph 53), the insert is any length including 12 amino acids long, and the AB toxin can be Shiga-like toxin (please refer to the entire specification particularly the abstract; paragraphs 6, 14, 17, 30, 31, 40, 44, 50, and 53; Examples).

However, Keener et al. does not teach a library comprising at least 100 protein species or the sequence of SLT-1.

For present claims 2-5 and 7, Garipey et al. teach polypeptide libraries comprising Shiga-like toxin A chain (SEQ ID NO: 1) and 1000 clones (please refer to the entire specification particularly the abstract; pages 2-3, 5-6, 8, 11, 15, 19; Figure 1).

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The claims would have been obvious because the substitution of one known element (library of unknown size and SLT without disclosure of the sequence) for another (library of known size and known sequence for SLT) would have yielded predictable results (library of specific size with at least part of the specific sequence of SLT) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

#### *Allowable Subject Matter*

26. The full-length sequence of SEQ ID NO: 1 with an insert between amino acids 248 and 267 or between amino acid residues 251 and 252 is free of the prior art.

#### *Conclusion*

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/  
Primary Examiner, Art Unit 1639